=> d his

(FILE 'HOME' ENTERED AT 16:12:31 ON 19 DEC 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 16:12:48 ON 19 DEC 2002

L1 13 S PTTG2
L2 230 S PITUITARY(W)TUMOR(W)TRANSFORM?(3A)GENE OR PTTG
L3 236 S L1 OR L2
L4 423766 S (INHIBIT? OR DIMINISH? OR DECREAS? OR SUPPRESS?)(6A)(TUMOR OR
L5 32 S L3 AND L4
L6 18 DUP REM L5 (14 DUPLICATES REMOVED)

=> d 1-18 au ti so ab l6

L6 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2002 ACS
IN Horne, Darci; Alvares, Christopher; Peres da Silva, Supriya; Vockley, Joseph G.
TI Gene expression profiles in hepatocellular carcinoma and metastatic liver cancer
SO PCT Int. Appl., 298 pp.
CODEN: PIXXD2
AB The present invention identifies the global changes in gene expression assocd. with liver cancer by examg. gene expression in tissue from normal liver, metastatic malignant liver and hepatocellular carcinoma (HCC). Gene signatures were obtained by hybridizing cDNA from liver samples mRNA onto the Affymetrix HuGeneFl array and the Human Hu35k set of arrays. There are 8479 genes and ESTs in the pos. Gene Signature for the HCC tumors, and a total of 23,233 genes and ESTs are included in the neg. Gene Signature of the HCC samples (e.g., all the genes that have been completely turned off during tumorigenesis, as well as those genes that are not usually expressed in liver tissue). A differential comparison of the genes and ESTs expressed in the normals and the two different types of liver tumors identifies a subset of the genes included in the pos. Gene Signatures that are uniquely expressed in each sample set. A no. of the tumor-expressing genes are closely examd. to det. if their expression patterns correlate with previous reports published in the literature, and to define a logical relationship between the gene and hepatocarcinogenesis. The present invention also identifies expression profiles which serve as useful diagnostic markers as well as markers that can be used to monitor disease states, disease progression, drug toxicity, drug efficacy and drug metab.

L6 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2002 ACS
IN Heaney, Anthony P.; Ishikawa, Hiroki; Yu, Run; Horwitz, Gregory A.; Zhang, Xun; Melmed, Shlomo
TI Compositions and methods of modulating angiogenesis by regulating the expression of **pituitary tumor transforming gene** (**PTTG**)
SO U.S. Pat. Appl. Publ., 75 pp., Cont.-in-part of U.S. Ser. No. 730,469.
CODEN: USXXCO
AB Disclosed is a method and compns. for modulating angiogenesis in a tissue comprising mammalian cells, including cells of human origin, in vitro or in vivo. Included are compns. comprising **PTTG** peptides, **PTTG** carboxyterminal peptide, or comprising a chimeric or fusion protein that contains a first **PTTG** carboxyterminal peptide segment and a second cellular uptake-enhancing peptide segment. The invention also relates to compns. comprising a **PTTG** peptide-encoding polynucleotide, a **PTTG** carboxyterminal-related polynucleotide, for example, a polynucleotide encoding a **PTTG**-C peptide or antisense **PTTG**-specific or **PTTG**-C-related oligonucleotides. Also disclosed are a method of enhancing wound healing and/or tissue regeneration and a method of limiting scar formation.

L6 ANSWER 3 OF 18 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AU Rogler, Charles E. (1); Rogler, Leslie E. (1); Carver, Robert (1); Harris, Thomas (1)
TI cDNA microarrays reveal downregulation of **pituitary tumor transforming gene** in a liver **tumor suppression** model.
SO Hepatology, (October, 2002) Vol. 36, No. 4 Part 2, pp. 702A. http://hepatology.aasldjournals.org/scripts/om.dll/serve?action=searchDB&searchDBfor=home&id=jhep. print.
Meeting Info.: 53rd Annual Meeting on the Liver BOSTON, MA, USA November 01-05, 2002
ISSN: 0270-9139.

L6 ANSWER 4 OF 18 MEDLINE DUPLICATE 1
AU Bernal Juan A; Luna Rosa; Espina Agueda; Lazaro Iciar; Ramos-Morales Francisco; Romero Francisco; Arias Carmen; Silva Augusto; Tortolero Maria; Pintor-Toro Jose A
TI *Human securin interacts with p53 and modulates p53-mediated* transcriptional activity and apoptosis.
SO NATURE GENETICS, (2002 Oct) 32 (2) 306-11.
Journal code: 9216904. ISSN: 1061-4036.
AB The **gene** PTTG1 (*encoding the* **pituitary tumor -transforming** 1 protein) is overexpressed in several different tumor types, is tumorigenic in vivo and shows transcriptional activity. The PTTG1 protein is cell-cycle regulated and was identified as the human securin (a category of proteins involved in the regulation of sister-chromatid separation) on the basis of biochemical similarities with the Pds1p protein of budding yeast and the Cut2p protein of fission yeast. To unravel the function of human securin in oncogenesis, we carried out a phage-display screening to identify proteins that interact with securin. Notably, we isolated the p53 **tumor suppressor**. Pull-down and co-immunoprecipitation assays demonstrated that p53 interacts specifically with securin both in vitro and in vivo. This interaction blocks the specific binding of p53 to DNA and inhibits its transcriptional activity. Securin also inhibits the ability of p53 to induce cell death. Moreover, we observed that transfection of H1299 cells with securin induced an accumulation of G2 cells that compensated for the loss of G2 cells caused by transfection with p53. We demonstrated the physiological relevance of this interaction in PTTG1-deficient human tumor cells (PTTG1(-/-)): both apoptotic and transactivating functions of p53 were potentiated in these cells compared to parental cells. We propose that the oncogenic effect of increased expression of securin may result from modulation of p53 functions.

L6 ANSWER 5 OF 18 MEDLINE DUPLICATE 2
AU Heaney Anthony P; Fernando Manory; Melmed Shlomo
TI Functional role of estrogen in pituitary tumor pathogenesis.
SO JOURNAL OF CLINICAL INVESTIGATION, (2002 Jan) 109 (2) 277-83.
Journal code: 7802877. ISSN: 0021-9738.
AB Pituitary hyperplasia and lactotroph replication are induced by estrogen. The product of the **pituitary tumor transforming gene** (**PTTG**) exhibits in vitro and in vivo transforming activity and induces basic bFGF secretion, thereby modulating pituitary angiogenesis and tumor formation. We demonstrated previously that pituitary **pttg** is induced by estrogen and bFGF, the latter being expressed in a concordant fashion with **pttg** in experimental and human pituitary adenomas. We now elucidate the role of estrogen in paracrine regulation of pituitary tumorigenesis by **PTTG**. Coincident with the circulating rat estradiol surge and maximal pituitary proliferation, pituitary **pttg** mRNA, bFGF, and VEGF expression increased approximately threefold during proestrus and estrus. Osmotic mini-pump coinfusion of estrogen and antiestrogen abrogated estrogen-induced pituitary **pttg** expression in vivo,

suppressed serum PRL concentrations by 88%, and attenuated prolactin-secreting pituitary tumor growth by 41% in rats. Antiestrogen treatment of primary human pituitary tumor cultures reduced **PTTG** expression approximately 65%. Pituitary **pttg**, bFGF, and VEGF are cyclically expressed during the rat estrus cycle, concordantly with estrogen levels. Because anti-estrogens reduced **PTTG** expression in human pituitary **tumors** in vitro and **suppressed** experimental **tumor** growth in vivo, concomitantly with reduced PRL secretion, these results indicate a role for selective antiestrogens in treating pituitary tumors.

L6 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2002 ACS
AU Takamura, Noboru
TI Molecular abnormalities of pituitary tumor
SO Naibunpi, Tonyobyoka (2002), 14(2), 138-143
CODEN: NATOFF; ISSN: 1341-3724
AB A review on gene mutations in pituitary tumor. The topics discussed are (1) clonality of pituitary tumors; (2) gene mutations in Gs protein, Ras, protein kinase C (PKC), and **pituitary tumor-transforming gene** (**PTTG**); (3) **tumor suppressor** gene mutations of MEN1, retinoblastoma (RB) gene, nm23, and p53; and (4) growth factor mutations of transforming growth factor-.alpha. (TGF-.alpha.) and fibroblast growth factor-4 (FGF-4).

L6 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2002 ACS
IN Stoika, Rostyslav; Horwitz, Gregory A.; Zhang, Xun; Melmed, Shlomo
TI Compositions and methods for modulating mammalian T-lymphocytes by targeted **pituitary tumor transforming gene** (**PTTG**) expression and/or function
SO PCT Int. Appl., 185 pp.
CODEN: PIXXD2
AB Disclosed is a method of **inhibiting neoplastic** cellular **proliferation** and/or transformation of mammalian T-lymphocyte cells, including cells of human origin, in vitro or in vivo. Also disclosed are methods of immunomodulating, i.e., inhibiting or inducing, the activation of T-lymphocytes by modulating **gene PTTG** (**pituitary tumor transforming gene**) expression and/or gene PTTG1 protein function. In vitro methods for screening substances for new immunosuppressing or immunoenhancing agents that modulate the activation of mammalian T-lymphocytes are disclosed. Also disclosed are useful compns. and kits. CDNA for human gene PTTG1 has been cloned based on sequence homol. with the rat **PTTG** gene. The rat and human genes and their encoded proteins have been investigated, including their mRNA expression in tissues and cell lines, transactivation of gene transcription, effects of overexpression on cell proliferation and tumor induction, regulation of human bFGF secretion, and identification of a human **PTTG** gene family. Gene PTTG1 and its encoded protein have transforming activity, in vitro and in vivo, which requires a proline-rich domain in the polypeptide C-terminal region. The transforming protein encoded by gene PTTG1 may function through SH3-mediated signal transduction. Human gene PTTG1 mRNA is overexpressed in most cancers, including tumors of the colon, breast, ovary, and myeloid lineages. Gene PTTG1 mRNA expression also increases upon T cell activation by anti-CD3 antibodies or phytohemagglutinin (PHA) in parallel with T cell proliferation, after IL-2 mRNA induction, and before cyclophilin mRNA induction. Immunosuppressants hydrocortisone and cyclosporin A inhibit PHA-stimulated gene PTTG1 expression and T cell proliferation in normal T cells, while cyclosporin A and TGF-.beta.1 inhibit gene PTTG1 mRNA induction in activated leukemia cells. MRNA expression of gene PTTG1 is cell cycle-dependent in both T cells and a T cell leukemia line, with highest expression in G2/M-phase cells. Transfection of PHA-activated T cells with gene PTTG1 DNA encoding the C-terminal polypeptide region decreased the amt. of S-phase cells and increased G2/M-phase cells.

L6 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2002 ACS
IN Heaney, Anthony P.; Ishikawa, Hiroki; Yu, Run; Horwitz, Gregory A.; Zhang, Xun; Melmed, Shlomo
TI Compositions and methods for modulating angiogenesis by regulated expression of **pituitary tumor transforming gene (PTTG)**
SO PCT Int. Appl., 183 pp.
CODEN: PIXXD2
AB Disclosed are compns. and methods of modulating angiogenesis in a tissue comprising mammalian cells, including cells of human origin, in vitro or in vivo. The compns. and methods also apply to enhancing wound healing and/or tissue regeneration and a method of limiting scar formation. CDNA for human **gene** PTTG1 (**pituitary tumor transforming gene**) has been cloned based on sequence homol. with the rat **PTTG** gene. The rat and human genes and their encoded proteins have been investigated, including their mRNA expression in tissues and cell lines, transactivation of gene transcription, effects of overexpression on cell proliferation and tumor induction, regulation of human bFGF secretion, and identification of a human **PTTG** gene family. Gene PTTG1 and its encoded protein have transforming activity, in vitro and in vivo, which requires a proline-rich domain in the polypeptide C-terminal region. The transforming protein encoded by gene PTTG1 may function through SH3-mediated signal transduction. Expression constructs with the C-terminal peptide of human gene PTTG1 block cell transformation, **inhibit tumor** formation in carcinoma cell lines and in nude mice, and suppress bFGF secretion. Human gene PTTG1 protein also exhibits angiogenic activity in assays using transfected cells.

L6 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2002 ACS
IN Horwitz, Gregory A.; Zhang, Xun; HeaneyAnthony, P.; Melmed, Shlomo
TI C-terminal peptides of the **PTTG** gene product and their use in **inhibition** of **neoplastic** cellular **proliferation** or transformation
SO PCT Int. Appl., 190 pp.
CODEN: PIXXD2
AB A method of **inhibiting neoplastic** cellular **proliferation** and transformation of mammalian cells using C-terminal peptides derived from the product of the **PTTG** (**pituitary tumor transforming gene**) **gene** is described. The peptides regulate the function of the protein and gene expression in a dominant neg. manner. The peptides may be used directly, as fusion proteins with uptake-promoting peptides, or expression vectors encoding the peptides may be used in gene therapy. The peptides may also increase the effectiveness of cytotoxic chemotherapeutic agents conventionally used to treat breast or ovarian cancers, thus allowing lower EDs of the agents to be administered. Kits comprising the inventive compns. are also disclosed for the treatment of neoplastic cellular proliferation in vitro or in vivo. Isolated **PTTG**-C peptides and **PTTG**-C-related polynucleotides are also disclosed, as are anti-**PTTG**-C-specific antibodies. Cloning and characterization of the **PTTG** gene and its role in neoplastic transformation is described. Two-hybrid assays showed that the **PTTG** gene product acted as a transcriptional activator. Deletion anal. identified the C-terminal region as important in regulating neoplastic transformation. This area is proline-rich and includes an SH3 domain.

L6 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2002 ACS
IN Prezant, Toni Rita; Heaney, Anthony P.; Melmed, Shlomo
TI **Pituitary tumor transforming gene** 2 (**PTTG2**) and its role in the regulation of expression of **pituitary tumor transforming gene** 1

SO PCT Int. Appl., 175 pp.
CODEN: PIXXD2

AB Disclosed is a method of **inhibiting neoplastic** cellular **proliferation** and/or transformation of mammalian breast or ovarian cells, including cells of human origin, in vitro or in vivo. The inventive method involves the use of **pituitary tumor transforming gene** 2 (**PTTG2**) product, which has the ability to regulate endogenous PTTG1 expression in a dominant neg. manner. In some embodiments, the invention is directed to gene-based treatments that deliver **PTTG2**-encoding polynucleotides to mammalian cells, whether in vitro or in vivo, to inhibit the endogenous expression of PTTG1. Other embodiments are directed to peptide-based treatments that deliver **PTTG2** peptide mols. to the cells, which inhibit endogenous PTTG1 expression and/or PTTG1 function. Kits useful in practicing the inventive method are also disclosed.

L6 ANSWER 11 OF 18 MEDLINE DUPLICATE 3
AU Heaney A P; Nelson V; Fernando M; Horwitz G
TI Transforming events in thyroid tumorigenesis and their association with follicular lesions.
SO JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, (2001 Oct) 86 (10) 5025-32.
Journal code: 0375362. ISSN: 0021-972X.

AB Thyroid tumors comprise a broad spectrum of neoplastic phenotypes, and distinct molecular events have been implicated in their pathogenesis. **Pituitary tumor transforming gene**, originally isolated from GH(4) pituitary cells, is tumorigenic in vivo, regulates basic fibroblast growth factor secretion, and is homologous to a securin **inhibitor** of chromatid separation. **Pituitary tumor transforming gene** 1 is expressed at low levels in several normal human tissues and is abundantly expressed in neoplasms, including colorectal carcinoma, where **pituitary tumor transforming gene** expression correlated highly with tumor invasiveness. As **pituitary tumor transforming gene** is regulated by E and as thyroid cancer shows a strong female preponderance, we examined **pituitary tumor transforming gene** 1 expression and action in human thyroid tumors and in normal human and rat thyroid cells. Increased **pituitary tumor transforming gene** 1 expression was evident early in thyroid tumors and was most abundantly expressed in a subset of thyroid hyperplasia, follicular adenomas, and follicular carcinomas (1.8-fold; $P < 0.0001$). **Pituitary tumor transforming gene** 1 overexpression in rat FRTL5 thyroid cells and in primary human thyroid cell cultures causes in vitro transformation and produces a dedifferentiated neoplastic phenotype. As **pituitary tumor transforming gene** 1 was abundantly overexpressed in follicular adenoma and follicular carcinoma, we propose that **pituitary tumor transforming gene** overexpression may play a role in the early molecular events leading to divergent development of follicular and papillary carcinoma.

L6 ANSWER 12 OF 18 SCISEARCH COPYRIGHT 2002 ISI (R)
AU Cushman L J; Camper S A (Reprint)
TI Molecular basis of pituitary dysfunction in mouse and human
SO MAMMALIAN GENOME, (JUL 2001) Vol. 12, No. 7, pp. 485-494.
Publisher: SPRINGER-VERLAG, 175 FIFTH AVE, NEW YORK, NY 10010 USA.
ISSN: 0938-8990.

L6 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2002 ACS
AU Tackels-Horne, Darci; Goodman, M. David; Williams, Amanda J.; Wilson, Daniel J.; Eskandari, Tara; Vogt, Lisa M.; Boland, Joseph F.; Scherf, Uwe; Vockley, Joseph G.
TI Identification of differentially expressed genes in hepatocellular

carcinoma and metastatic liver tumors by oligonucleotide expression profiling

SO Cancer (New York, NY, United States) (2001), 92(2), 395-405
CODEN: CANCAR; ISSN: 0008-543X

AB The characterization of differentially expressed genes between cancerous and normal tissues is an important step in the understanding of tumorigenesis. Global gene expression profiling with microarrays has now offered a powerful tool to measure the changes of thousands of genes in any carcinoma tissues in an effort to identify these key disease-related genes. To compare the gene expression of a primary liver carcinoma, metastatic carcinoma to the liver, and normal liver, the authors analyzed tissue from six primary hepatocellular carcinomas (HCCs), five colorectal adenocarcinoma metastases to the liver, and eight normal livers. Samples were processed from total RNA to fragmented cRNA and hybridized onto Affymetrix GeneChip expression arrays. Analyses were performed to det. the consensus pattern of gene expression for primary liver carcinoma, metastatic liver carcinoma, and normal liver tissue and their changes in expression level. In hepatocellular carcinoma, 842 genes were overexpressed, and 393 genes were underexpressed in comparison with genes of normal liver tissue. Of note, 7 of the 20 most increased identified known genes previously have been assocd. with liver carcinoma or other types of cancers. The 13 addnl. identified genes until now have not previously shown strong assocn. with cancers. Furthermore, the authors identified 42 genes and 24 expressed sequence tags that are expressed at a significant level in both HCC and metastatic tumors, presenting a list of marker genes indicative of cancerous liver tissue. In this study, genes that can be involved in the prodn. of and maintenance of hepatic carcinomas were identified. These data offer new insight into genes that are potentially important in the pathogenesis of liver carcinoma, as well as addnl. targets for new strategies for cancer therapy and treatment.

L6 ANSWER 14 OF 18 SCISEARCH COPYRIGHT 2002 ISI (R)

AU Lloyd R V (Reprint)

TI Molecular pathology of pituitary adenomas

SO JOURNAL OF NEURO-ONCOLOGY, (SEP 2001) Vol. 54, No. 2, pp. 111-119.
Publisher: KLUWER ACADEMIC PUBL, SPUIBOULEVARD 50, PO BOX 17, 3300 AA DORDRECHT, NETHERLANDS.
ISSN: 0167-594X.

AB A great deal of knowledge about anterior pituitary development, the pathogenesis of pituitary tumor and pituitary tumor progression has accumulated during the past decade. The role of multiple genes and gene products in pituitary development and the relationship of these genes to postnatal pituitary function and pituitary tumor development are being actively explored.

Recent studies indicate that genes important in pituitary development do not contribute to pituitary tumorigenesis. However, mutations and other genetic alterations in these genes often lead to pituitary hypofunction. Many oncogenes and **tumor suppressor** genes that contribute to pituitary tumorigenesis have been described. There is a growing body of evidence showing that cellular and molecular changes in cyclins and cyclin-dependent kinase inhibitors contribute to pituitary tumorigenesis. Finally, recent comparative genomic hybridization studies show that many more genes that are important in pituitary tumorigenesis and tumor progression have yet to bebreak discovered.

L6 ANSWER 15 OF 18 MEDLINE DUPLICATE 4

AU Farrell W E; Clayton R N

TI Molecular pathogenesis of pituitary tumors.

SO FRONTIERS IN NEUROENDOCRINOLOGY, (2000 Jul) 21 (3) 174-98. Ref: 97
Journal code: 7513292. ISSN: 0091-3022.

AB Pituitary tumors are the result of a monoclonal outgrowth where the intrinsic genetic defects involve oncogenes, **tumor suppressor** genes (TSG), and most likely genes responsible for differentiation. In addition, hypothalamic and intrapituitary derived

growth factors are imposed upon these aberrant cells, contributing to their growth characteristics. While histological examination will not identify those tumors likely to progress toward an invasive phenotype or those destined toward recurrence recent advances in the molecular pathology of these tumors holds significant promise for prediction of recurrence and the design of novel treatment strategies. Moreover, emerging data clearly indicate that different molecular mechanisms are involved in the pathogenesis of the various pituitary tumor subtypes. Until recently the gsp oncogene was the only oncogene significantly associated with pituitary tumors; however, emerging data have describe a role for **PTTG** and cyclin D1 in pituitary tumorigenesis. For known and putative TSG loci, allelic losses on the long arms of chromosomes 10, 11, and 13 are significantly associated with the transition from the noninvasive to the invasive and metastatic phenotype, while losses on chromosome 9p occur early in pituitary tumorigenesis. Studies of known TSG at these loci, including the menin gene and RB1, would suggest a limited role, if any, in pituitary tumors. However, loss of pRB is evident in a proportion of somatotropinomas but is not associated with allelic loss of an RB1 intragenic marker. The gene encoding p16/CDKN2A is neither deleted nor mutated in pituitary tumors; however, its associated CpG island is frequently methylated and is associated with a loss of p16 protein expression. Allelic losses on chromosome 9p, frequent methylation, and loss of p16 protein appear as early changes in nonfunctional tumors, whereas they are infrequent events in somatotropinomas. The functional consequence of enforced expression of p16/CDKN2A in the mouse corticotroph cell line AtT20 has shown that it is responsible for a profound reduction in cell proliferation and the mechanism is a G(1) arrest, mimicking the in vivo role of this cell cycle regulator in most tissues. The combined data from several groups show that the allelic losses reported at known TSG loci are not accompanied by mutation in the retained allele. However, since abnormal methylation patterns may precede and predispose toward genetic instability this could account for the allelic losses on these chromosomes. Equally, since DNA methylation may lead to reduced expression of a gene it might also account for the reduced expression of as yet unidentified TSGs implicated in pituitary tumorigenesis. Collectively these studies hold significant promise as markers predictive of tumor behavior and point to novel treatment strategies, which may include the reactivation of TSGs that are intact but silenced through epigenetic mechanisms.

L6 ANSWER 16 OF 18 MEDLINE DUPLICATE 5
AU Heaney A P; Melmed S
TI New pituitary oncogenes.
SO ENDOCRINE-RELATED CANCER, (2000 Mar) 7 (1) 3-15. Ref: 101
Journal code: 9436481. ISSN: 1351-0088.
AB Pituitary tumors are common monoclonal neoplasms which cause considerable morbidity and mortality. Several molecular events underlying pituitary tumorigenesis have been elucidated in recent years, but no tumor marker has clearly emerged which assists clinical and therapeutic decisions. Activating mutations and loss of inactivating mutations, together with hypothalamic hormones, circulating hormones, growth factors and cytokines cooperatively ensure the inexorable expansion of the initial mutated pituitary cell clone. This review describes new developments in our understanding of the molecular mechanisms involved in the pathogenesis of pituitary tumors. The availability of molecular probes will allow the early prediction of tumor behavior, identify targets for designing subcellular pituitary tumor therapy and provide novel approaches to pituitary tumor management.

L6 ANSWER 17 OF 18 MEDLINE
AU Heaney A P; Melmed S
TI Pituitary tumour transforming gene: a novel factor in pituitary tumour formation.

SO BAILLIERES BEST PRACTICE & RESEARCH. CLINICAL ENDOCRINOLOGY & METABOLISM, (1999 Oct) 13 (3) 367-80. Ref: 57
Journal code: 100957144. ISSN: 1521-690X.

AB Although pituitary tumours are common monoclonal neoplasms, they rarely metastasize outside the pituitary fossa, even though they cause considerable morbidity and mortality. Many molecular events underlying pituitary tumourigenesis have been elucidated in recent years, but no clear tumour marker has emerged that assists clinical decision-making with regard to appropriate therapy. Activating mutations and a loss of inactivating mutations, together with hypothalamic hormones, circulating hormones, growth factors and cytokines, co-operatively ensure the inexorable expansion of the initial mutated pituitary cell clone. We have recently described a novel oestrogen-regulated activating oncogene, pituitary tumour transforming gene (**PTTG**), which is potently transforming in vitro and in vivo, regulates basic fibroblast growth factor secretion and inhibits chromatid separation. In experimental animal pituitary tumour models, increased **PTTG** expression occurs early in cell transformation (from normal to hyperplastic cell), **PTTG** overexpression being observed in 99% of pituitary tumours. **PTTG** presents an attractive target for designing subcellular pituitary tumour therapy, and an increased understanding of its role and that of other genetic events in pituitary tumorigenesis may provide novel approaches to pituitary tumour management.

L6 ANSWER 18 OF 18 MEDLINE DUPLICATE 6

AU Pei L; Melmed S

TI Isolation and characterization of a **pituitary tumor-transforming gene** (**PTTG**).

SO MOLECULAR ENDOCRINOLOGY, (1997 Apr) 11 (4) 433-41.
Journal code: 8801431. ISSN: 0888-8809.

AB Pathogenesis of tumor formation in the anterior pituitary has been intensively studied, but the common mechanism involved in pituitary cell transformation and tumorigenesis remains elusive. In this study, we used mRNA differential display PCR to identify mRNAs that are differentially expressed in rat pituitary tumor cells compared with normal pituitary tissue. An mRNA exclusively expressed in pituitary tumor but not in normal pituitary was characterized. Using this pituitary tumor-specific PCR product as a probe to screen a cDNA library constructed from rat pituitary tumor GH4 cells, a cDNA of 974 bp was isolated. This cDNA encodes a novel protein of 199 amino acids, which contains no well characterized functional motifs. The mRNA of this cDNA is detected in normal adult testis and in embryonic liver, where the transcript is about 300 bp shorter and expressed at a much lower level than that detected from pituitary tumor cells. Overexpression of this protein in mouse 3T3 fibroblasts shows that it **inhibits** cell **proliferation** and induces cell transformation in vitro. Injection of transfected 3T3 cells into athymic nude mice resulted in tumor formation within 3 weeks in all animals. These results indicate that pituitary tumor cells express a unique and potent transforming gene (**PTTG**), which may play a role in pituitary tumorigenesis.

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L7            4 L1 AND L4

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PROCESSING COMPLETED FOR L7
L8            4 DUP REM L7 (0 DUPLICATES REMOVED)

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L8   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2002 ACS
IN   Stoika, Rostyslav; Horwitz, Gregory A.; Zhang, Xun; Melmed, Shlomo
TI   Compositions and methods for modulating mammalian T-lymphocytes by
     targeted pituitary tumor transforming gene (PTTG) expression and/or
     function
SO   PCT Int. Appl., 185 pp.
     CODEN: PIXXD2

L8   ANSWER 2 OF 4  CAPLUS  COPYRIGHT 2002 ACS
IN   Heaney, Anthony P.; Ishikawa, Hiroki; Yu, Run; Horwitz, Gregory A.; Zhang,
     Xun; Melmed, Shlomo
TI   Compositions and methods for modulating angiogenesis by regulated
     expression of pituitary tumor transforming gene (PTTG)
SO   PCT Int. Appl., 183 pp.
     CODEN: PIXXD2

L8   ANSWER 3 OF 4  CAPLUS  COPYRIGHT 2002 ACS
IN   Horwitz, Gregory A.; Zhang, Xun; HeaneyAnthony, P.; Melmed, Shlomo
TI   C-terminal peptides of the PTTG gene product and their use in
     inhibition of neoplastic cellular proliferation
     or transformation
SO   PCT Int. Appl., 190 pp.
     CODEN: PIXXD2

L8   ANSWER 4 OF 4  CAPLUS  COPYRIGHT 2002 ACS
IN   Prezant, Toni Rita; Heaney, Anthony P.; Melmed, Shlomo
TI   Pituitary tumor transforming gene 2 (PTTG2) and its role in the
     regulation of expression of pituitary tumor transforming gene 1
SO   PCT Int. Appl., 175 pp.
     CODEN: PIXXD2


=> d bib 1-4 l8

L8   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2002 ACS
AN   2001:851361  CAPLUS
DN   136:622
TI   Compositions and methods for modulating mammalian T-lymphocytes by
     targeted pituitary tumor transforming gene (PTTG) expression and/or
     function
IN   Stoika, Rostyslav; Horwitz, Gregory A.; Zhang, Xun; Melmed, Shlomo
PA   Cedars-Sinai Medical Center, USA
SO   PCT Int. Appl., 185 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
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     PATENT NO.         KIND  DATE           APPLICATION NO.  DATE
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	US 2000-687911	A	20001013		
	US 2000-730469	A	20001204		
	US 2001-777422	A	20010205		
	US 2001-854326	A	20010511		
	US 1996-31338P	P	19961121		
	WO 1997-US21463	W	19971121		
	US 1999-894251	A2	19990723		

L8 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 2001:851203 CAPLUS
DN 136:691
TI Compositions and methods for modulating angiogenesis by regulated expression of pituitary tumor transforming gene (PTTG)
IN Heaney, Anthony P.; Ishikawa, Hiroki; Yu, Run; Horwitz, Gregory A.; Zhang, Xun; Melmed, Shlomo
PA Cedars-Sinai Medical Center, USA
SO PCT Int. Appl., 183 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001087935	A2	20011122	WO 2001-US15437	20010512
	WO 2001087935	A3	20020808		

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HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

	US 2002147162	A1	20021010	US 2001-777422	20010205
PRAI	US 2000-569956	A	20000512		
	US 2000-687911	A	20001013		
	US 2000-730469	A	20001204		
	US 2001-777422	A	20010205		
	US 2001-854326	A	20010511		
	US 1996-31338P	P	19961121		
	WO 1997-US21463	W	19971121		
	US 1999-894251	A2	19990723		

L8 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 2001:851202 CAPLUS
DN 136:4255
TI C-terminal peptides of the PTTG gene product and their use in **inhibition** of **neoplastic** cellular **proliferation** or transformation
IN Horwitz, Gregory A.; Zhang, Xun; HeaneyAnthony, P.; Melmed, Shlomo
PA Cedars-Sinai Medical Center, USA
SO PCT Int. Appl., 190 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001087934	A2	20011122	WO 2001-US15254	20010512
	WO 2001087934	A3	20020530		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002147162	A1	20021010	US 2001-777422	20010205
PRAI	US 2000-569956	A	20000512		
	US 2000-687911	A	20001013		
	US 2000-730469	A	20001204		
	US 2001-777422	A	20010205		
	US 1996-31338P	P	19961121		
	WO 1997-US21463	W	19971121		
	US 1999-894251	A2	19990723		

L8 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS
AN 2001:850858 CAPLUS
DN 136:4254
TI *Pituitary tumor transforming gene 2* (**PTTG2**) *and its role in the regulation of expression of pituitary tumor transforming gene 1*
IN Prezant, Toni Rita; Heaney, Anthony P.; Melmed, Shlomo
PA Cedars-Sinai Medical Center, USA
SO PCT Int. Appl., 175 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001087039	A2	20011122	WO 2001-US15255	20010512
	WO 2001087039	A3	20020321		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002147162	A1	20021010	US 2001-777422	20010205
	AU 2001063059	A5	20011126	AU 2001-63059	20010512
PRAI	US 2000-730469	A	20000120		
	US 2000-569956	A	20000512		
	US 2000-687911	A	20001013		
	US 2001-777422	A	20010205		
	US 1996-31338P	P	19961121		
	WO 1997-US21463	W	19971121		
	US 1999-894251	A2	19990723		
	WO 2001-US15255	W	20010512		

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